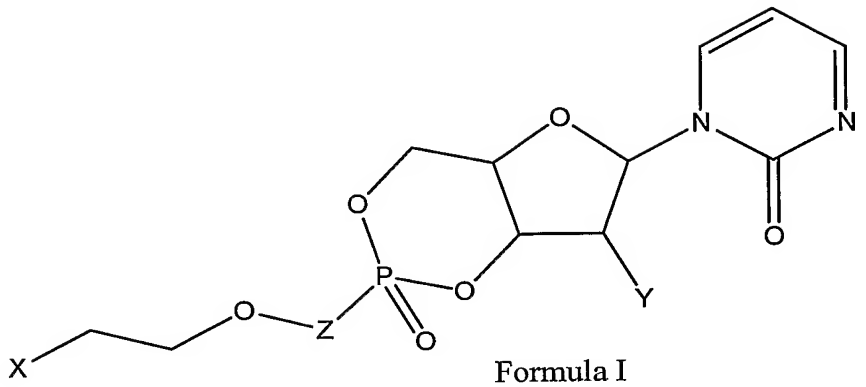
Claims

What is claimed is:

1. An isolated compound of Formula I:



Formula I

wherein,

each X is independently NR^1R^2, or $NR^1R^2R^{3+}$;

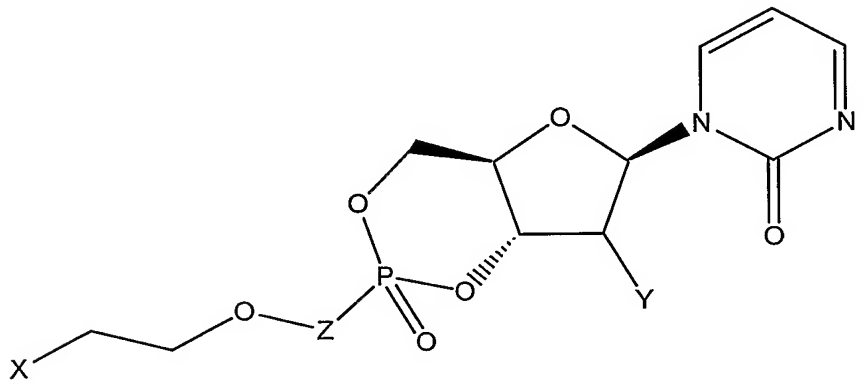
each R^1, R^2 and R^3 is independently H or alkyl;

each Y is independently H, OH, or halogen; and

each Z is independently a bond or –P(O)(OH)-O-;

or pharmaceutically acceptable salt or hydrate thereof.

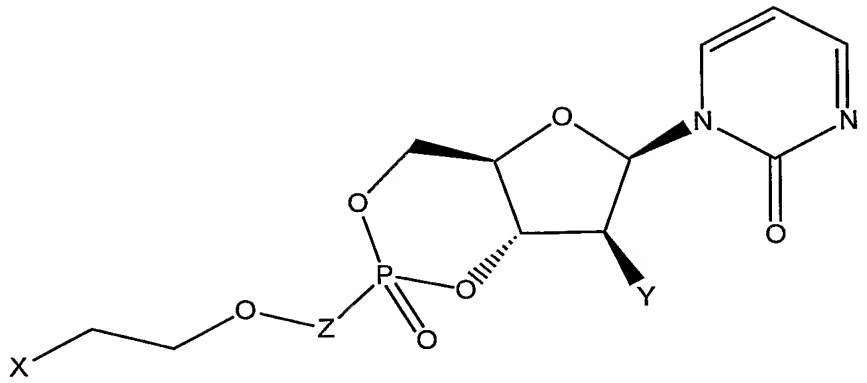
2. The compound of claim 1 having Formula II:



Formula II

wherein X, R^1, R^2, R^3, Y and Z are as defined in claim 1.

3. The compound of claim 2 having Formula III,



Formula III

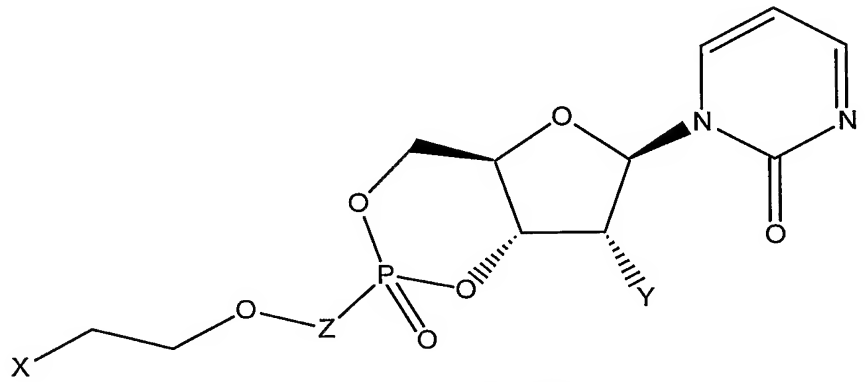
wherein X, R^1, R^2, R^3, Y and Z are as defined in claim 1.

4. The compound of claim 3, wherein Y is halogen.

5. The compound of claim 3, wherein Y is fluoro.

6. The compound of claim 3, wherein Y is hydrogen.

7. The compound of claim 1, having Formula IV:



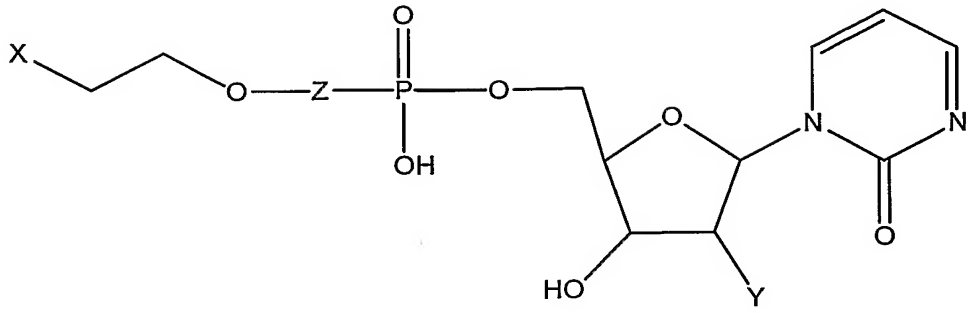
Formula IV

wherein X, R^1; R^2, R^3 and Z are as defined in claim 1 and Y is OH.

8. The compound of claim 1, wherein X is NH_2.

9. The compound of claim 1, wherein X is $(NMe_3)^+$.

10. An isolated compound of Formula V:



Formula V

wherein,

each X is independently NR^1R^2, or $NR^1R^2R^{3+}$;

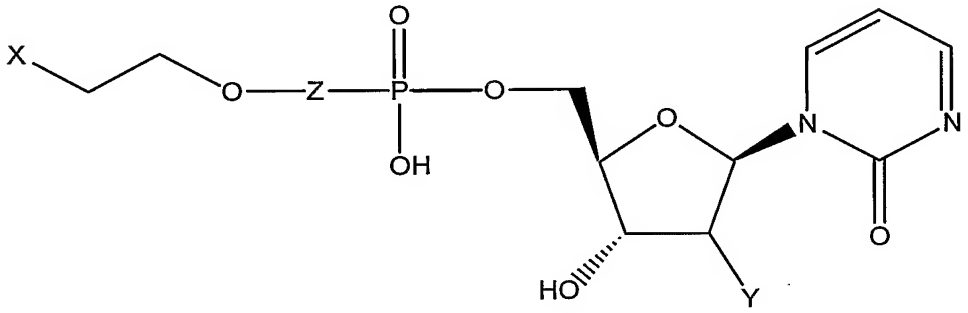
each R^1, R^2 and R^3 is independently H or alkyl;

each Y is independently H, OH, or halogen; and

each Z is independently a bond or –P(O)(OH)-O-;

or pharmaceutically acceptable salt or hydrate thereof.

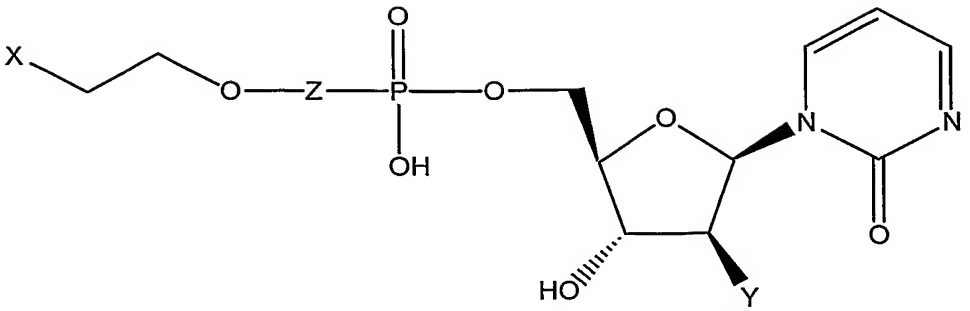
11. The compound of claim 10 having Formula VI:



Formula VI

wherein X, R^1, R^2, R^3, Y and Z are as defined in claim 10.

12. The compound of claim 11 having Formula VII,



Formula VII

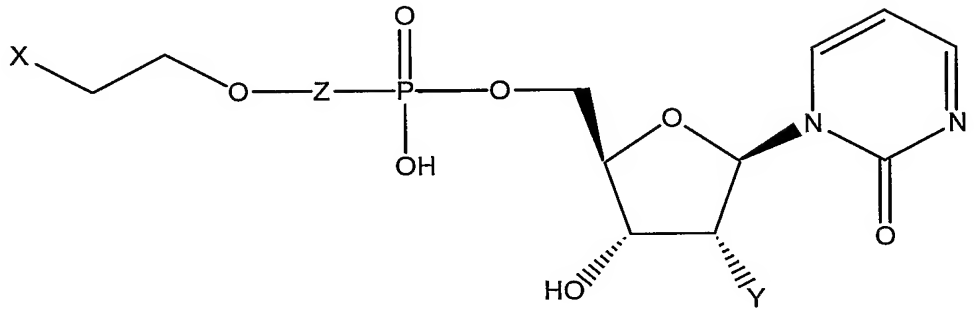
wherein X, R^1, R^2, R^3, Y and Z are as defined in claim 11.

13. The compound of claim 12, wherein Y is halogen.

14. The compound of claim 13, wherein Y is fluoro.

15. The compound of claim 12, wherein Y is hydrogen.

16. The compound of claim 10, having Formula VIII:



Formula VIII

wherein X, R^1; R^2, R^3 and Z are as defined in claim 10 and Y is OH.

17. The compound of claim 10, wherein X is NH_2.

18. The compound of claim 10, wherein X is $(NMe_3)^+$.

19. A composition comprising a therapeutically effective amount of a compound according to claim 1 or 10and a pharmaceutically acceptable carrier.

20. The composition according to claim 19, further comprising an additional therapeutic agent.

21. The composition of claim 20, wherein the additional agent is an anticancer agent.

22. A method of treating a DNA methyl transferase (DNMT) mediated disease, disease symptom or condition comprising administration to a subject in need of such treatment a compound according to claim 1 or 10.

23. The method of claim 22, wherein the disease, disease symptom or condition involves hypermethylation of DNA.

24. The method of claim 22, wherein the administration is by oral administration.

25. A method of treating a DNA methyl transferase (DNMT) mediated disease, disease symptom or condition comprising administration to a subject in need of such treatment a composition according to claim 19.

26. The method of claim 25, wherein the disease, disease symptom or condition involves hypermethylation of DNA.

27. The method of claim 25, wherein the administration is by oral administration.

28. A method of assessing the effect of a test compound on methylation of DNA in a cell comprising: (i) contacting a test compound with a cell that exhibits DNA methylation and measuring the methylation of DNA in the cell; (ii) contacting a compound of claim 1 or 10 with a cell that exhibits DNA methylation; and measuring the methylation of DNA in the cell; and (iii) comparing the results of step (i) with the results of step (ii).

29. The method of claim 28 wherein the cell comprises a hypermethylated nucleic acid molecule.

30. The method of claim 28 wherein the cell comprises a CpG dinucleotide.

31. The method of claim 28 wherein the cell is a mammalian tumor cell.

32. A method of reversing DNA methylation in a cell, comprising administering to a cell a therapeutically effective amount of a compound of claim 1 or 10.

33. The method of claim 32, wherein the cell is in a subject.

34. A method of treating cancer in a subject comprising administering an effective amount of a compound according to claim 1 or 10.

35. The method of claim 34, wherein the cancer is ovarian, breast, rectal, lung, prostate, pancreatic, bladder, solid tumor or a tumor having a silenced tumor suppressor gene.

36. The method of claim 34, further comprising an additional anticancer agent.

37. The method of claim 34, further comprising an anti-nausea or an anti-anemia agent.

38. A kit comprising a compound of claim 1 or 10 and instructions for in vitro use of the compound.

39. The kit of claim 38, wherein the in vitro use is screening for demethylation of a hypermethylated DNA.

40. A kit comprising a compound of claim 1 or 10 and instructions for administration to a subject.

41. The kit of claim 40, wherein the subject is in need of treatment for a hypermethylated DNA mediated disease, disease symptom or condition.

42. The kit of claim 40, wherein the subject is in need of treatment for a hyperproliferative disease, disease symptom or condition.

43. The kit of claim 40, wherein the subject is in need of treatment for cancer.

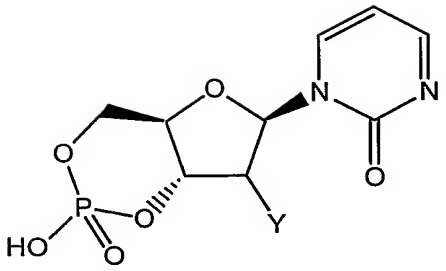
44. The kit of claim 40, wherein the subject is a human.

45. The kit of claim 40, wherein the subject is a rat or mouse.

46. The kit of claim 40, wherein the administration is oral.

47. The kit of claim 40, wherein the administration is intravenous or intraperitoneal.

48. A method of making a compound of Formula I in claim 1, comprising converting a compound of Formula B, wherein Y is H, OH, O-PG, or halo; and PG is a protecting group:



Formula B

to a compound of formula I in claim 1.

49. The method of claim 48, wherein the process further includes converting the compound of Formula B to the corresponding diphosphate.

50. The method of claim 48, wherein the process further includes a removal of an oxygen- or nitrogen-protecting group.